Upon entry of an Amendment filed April 14, 1997, all claims of copending U.S. application serial no. 08/398,852 are directed to peripheral neuropathy. Since all pending claims in Serial No. 08/398,852 are now drawn to treatment of the peripheral nervous system and all claims in this application serial no. 08/398,852 are drawn to treatment of the central nervous system, it is believed that the claims in the respective applications are patentably distinct. Therefore, applicant requests that this provisional obviousness-type double patenting rejection be withdrawn.

III. Rejection under 35 U.S.C. § 112, first paragraph

Claims 1-4, 7-11 and 14-18 are rejected under 35 U.S.C. 112, first paragraph, for allegedly not providing the full scope of enablement because the specification, "while being enabling for a method of parenteral administration of IGF-I, IGF-II or a combination of both IGF-I and II for the treatment of locus ceruleus noradrenergic neurons ablation by 6-hydroxydopamine, does not reasonably provide the full scope of enablement for parenteral administration of IGF-I or IGF-II, for effecting any changes in the central nervous system (CNS) or spinal cord and treating any disorders or diseases in the brain." Applicant respectfully traverses this rejection.

Claims 7 and 14 (directed to a method of treating AIDS dimentia) are withdrawn, without prejudice, by the above amendment and as such the rejection with respect to those claims is moot.

Applicants contend that the specification, as well as the state of the art as demonstrated by scientific publications, enables the invention claimed in the pending claims. The examples of

applicant's specification demonstrate that IGF-I or IGF-II can be parenterally administered *in vivo* to effect a change in the biochemistry and function of the brain and spinal cord. This result has been specifically demonstrated for treatment of the metabolic disorder of diabetes in rat (Example II) and treatment of an impaired behavior resulting from a brain lesion in rat (Example III). These results demonstrate that the parenteral administration of IGF-I and IGF-II can effect changes in brains of rats, a model which is reasonably predictive of the inventive methods applicability to a wide range of brain disorders and diseases.

The Examiner, nevertheless, asserts that applicant's examples do not demonstrate treatment of the various types of nerve tissues found in the brain and spinal cord. The applicability of such treatment to a wide variety of brain and spinal cord tissues is, however, clearly demonstrated in several scientific references. The references of Mooney et al. and Thornton et al. (submitted with the accompanying Information Disclosure Statement) indicate that the infusion of IGF-I into the ventricles of the brain prevents age-dependent loss of memory. Moreover, even the reference cited by the Examiner -- Lewis et al.-- provides examples of *in vitro* testing and intercranial administration of IGF affecting a wide range of brain tissues. Additionally, Gluckman et al. (1992) shows that the intercranial administration of IGF-I can prevent the death of 80% of brain neurons following hypoxic-ischemic brain injury.

Note that these reference do lack an enabling description of parenteral administration, since they only demonstrate *in vitro* use or intercranial administration. However, what the references do show is that once the IGF is within the blood-brain barrier, it effects a wide variety of tissues. As such, it can be reasonably predicted that IGF-I and II will be effective in treating a wide variety of diseases or disorders of the central nervous system.

In view of the above remarks, the rejection under 35 U.S.C. § 112, first paragraph, should be withdrawn.

IV. Rejection under 35 U.S.C. § 102(e) based on Lewis et al.

Claims 1-6, 8-13, and 15-18 are rejected under 35 U.S.C. 102(e) as allegedly being anticipated by Lewis et al., U.S. Patent No. 5,093,317. Applicant respectfully traverses this rejection.

Lewis et al. is of the view that the transfer of molecules across the blood-brain barrier is difficult (see Background of Invention). The examples of Lewis et al. fail to demonstrate any IGF molecule can act across the blood-brain barrier. Instead, the Lewis et al. examples are directed to *in vivo* administration of IGF that requires making a hole in the skull and injecting IGF directly into the brain -- a highly invasive procedure. Lacking any showing of an IGF acting across the blood-brain barrier, Lewis et al. does not provide an enabling disclosure that could possibly anticipate applicant's claimed invention.

Therefore, applicant respectfully submits that Lewis et al. does not anticipate applicant's invention and the rejection under 35 U.S.C. § 102(e) should be withdrawn.

In view of the foregoing amendment and remarks, applicant respectfully submits that all outstanding rejections are overcome and believes that this case is in condition for allowance. If the Examiner has any questions or comments regarding this application, he is invited to telephone the undersigned assignee's representative.

Respectfully submitted,

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June 20, 1997